UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,888	04/06/2007	Drew Pardoll	62763(71699)	4102

49383 7590 07/08/2010

EDWARDS ANGELL PALMER & DODGE LLP
P.O. BOX 55874
BOSTON, MA 02205

EXAMINER	
GIBBS, TERRA C	
ART UNIT	PAPER NUMBER
1635	
MAIL DATE	DELIVERY MODE
07/08/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,888	PARDOLL ET AL.	
	Examiner	Art Unit	
	TERRA C. GIBBS	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2010 and 22 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *1-19 and 23-31* is/are withdrawn from consideration.

5)☒ Claim(s) *32 and 33* is/are allowed.

6)☒ Claim(s) *20-22 and 34-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 August 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *August 9, 2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to Applicant's Election filed March 22, 2010 and Applicant's Amendment and Remarks filed April 29, 2010.

Claims 32 and 36 have been amended.

Claims 1-36 are pending in the instant application.

Election/Restrictions

Applicant's election of Group III, claims 20-22 and 32-36 in the reply filed on March 22, 2010 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-19 and 23-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. As noted above, because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election **without** traverse.

Accordingly, claims 20-22 and 32-36 have been examined on the merits.

The requirement is still deemed proper and is therefore made FINAL.

Response to Amendment

Applicant's Amendment and Remarks filed April 29, 2010 is acknowledged. It is noted that the instant application is fully compliant with the sequence rules and requirements of 37 CFR § 1.821-1.825.

Information Disclosure Statement

Applicant's information disclosure statement filed August 9, 2006 is acknowledged. The submission is in compliance with the provisions of 37 CFR §1.97. Accordingly, the Examiner has considered the information disclosure statement, and a signed copy is enclosed herewith.

The listing of references in the specification at pages 50-52 is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Drawings

The drawings filed on August 9, 2006 are acknowledged. The drawings are objected to because the description of the drawings indicates that such material may very well be critical to determining whether there exists adequate description and enablement of the instant invention. In brief, Figure 3 is sufficiently poor enough that it

is difficult to determine what is actually being described. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the Examiner, the Applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20-22 and 34-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter

which applicant regards as the invention. The claims are rejected because they recite the term, "MINOR" The term, "MINOR" is indefinite and the metes and bounds of the claims cannot be determined since abbreviations often have more than one meaning. Insertion of the full name of the mitogen induced nuclear orphan receptor (MINOR) would overcome the instant rejection.

Additionally, claim 36 is rejected because the claim recites, "(a) obtaining dendritic cells from the individual" and "(b) causing the dendritic cells to express the antigen". There is insufficient antecedent basis for these limitations in the claim. Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20-22, 34, and 35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a dendrite cell-based vaccine comprising dendritic cells expressing MINOR siRNA comprising SEQ ID NO:2 and SEQ ID NO:3 or a population of dendritic cells for use in vaccination of a subject, wherein the population of dendritic cells comprise SEQ ID NO:2 and SEQ ID NO:3, does not reasonably provide enablement for a dendrite cell-based vaccine comprising dendritic cells expressing siRNAs having substantial sequence homology to MINOR or a population of dendritic cells for use in vaccination of a subject, wherein the population of dendritic cells comprise an agent that inhibits MINOR expression. The specification

does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This is a scope enablement rejection.

There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue. These factors have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). Wands states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and the breadth of the claims:

The instant claims are drawn to a dendrite cell-based vaccine comprising dendritic cells expressing siRNAs having substantial sequence homology to MINOR or a population of dendritic cells for use in vaccination of a subject, wherein the population of dendritic cells comprise an agent that inhibits MINOR expression. The broadness of the claims implies a dendrite cell-based vaccine comprising dendritic cells expressing *any* siRNA having substantial sequence homology to the MINOR gene or *any* agent that inhibits MINOR expression. The nature of the invention, therefore, requires the knowledge of using dendrite cell-based vaccines in a subject.

The amount of direction or guidance and presence/absence of working examples:

Applicants disclose a dendrite cell-based vaccine comprising dendritic cells expressing MINOR siRNA comprising SEQ ID NO:2 and SEQ ID NO:3 and a population of dendritic cells for use in vaccination of a subject, wherein the dendritic cells comprise SEQ ID NO:2 and SEQ ID NO:3.

The specification as filed does not provide sufficient guidance or appropriate examples that would enable a skilled artisan to make a dendrite cell-based vaccine comprising dendritic cells expressing *any* siRNA having substantial sequence homology to MINOR. Additionally, a person skilled in the art would recognize that the use of dendritic-based vaccines is unpredictable. Thus, although the specification discloses a dendrite cell-based vaccine comprising dendritic cells expressing MINOR siRNA comprising SEQ ID NO:2 and SEQ ID NO:3 and a population of dendritic cells for use in vaccination of a subject, wherein the dendritic cells comprise SEQ ID NO:2 and SEQ ID NO:3, such a disclosure would not be considered enabling for a dendrite cell-based vaccine comprising dendritic cells expressing *any* siRNA having substantial sequence homology to MINOR or *any* agent that inhibits MINOR expression since the state of the art of dendrite cell-based vaccines is highly unpredictable. For further explanation, see discussion below.

The state of the prior art and the predictability or unpredictability of the art:

The claimed invention is a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

In regards to a dendrite cell-based vaccine comprising dendritic cells expressing siRNAs having substantial sequence homology to MINOR or an agent that inhibits MINOR expression, Applicant and the art has shown a high level of unpredictability regarding dendrite cell-based vaccines, including those DC based vaccines comprising an agent that inhibits MINOR. For example, Applicants teach:

> "It now appears that DC vaccines can elicit strong immune responses, but they are limited, in part, by their short lifespan *in vivo*";
>
> "Little is known about regulation of DC lifespan"; and
>
> "Extending the longevity of DCs would allow for their improved immunogenicity"

Similarly, the art (Wang et al., Blood, March 26, 2009 Vol. 113, No. 13, pages 2906-2913) teaches:

> "Although many advances have been made in understanding the nature of antigen processing and presentation, the genes that are important for regulating DC lifespan have not been well understood"; and
>
> "DCs have a short lifespan after activation *in vitro* and *in vivo*"

The art of Wang et al. also teach that mice vaccinated with DCs expressing MINOR siRNA ultimately died, and there was no significant difference in long-term survival, however inhibition of MINOR expression in the DC vaccines lead to a significant delay in tumor progression (see Figure 4).

The prior art of Hermans et al. (Journal of Immunology, 2000 Vol. 164, pages 3095-3101) generally teaches that although dendritic cells are critical for initiating immune responses, they are relatively short lived *in vitro* and *in vivo* and their transience affects their potential for therapeutic use.

The level of skill in the art:

The relative skill of those in the art is considered to be high, being a graduate student or post-doctoral fellow in a biological science.

The quantity of experimentation necessary:

A review of the instant application finds adequate guidance for a dendrite cell-based vaccine comprising dendritic cells expressing MINOR siRNA comprising SEQ ID NO:2 and SEQ ID NO:3 or a population of dendritic cells for use in vaccination of a subject, wherein the dendritic cells comprise SEQ ID NO:2 and SEQ ID NO:3. Although, Applicants clearly recognize the potential of a dendrite cell-based vaccine comprising dendritic cells expressing an agent which inhibits MINOR expression, Applicants only teach the ordinary artisan how to effectively make and use a dendrite cell-based vaccine comprising dendritic cells expressing MINOR siRNA comprising SEQ ID NO:2 and SEQ ID NO:3. No technical guidance or exemplary disclosure is provided regarding the use of any other agent which inhibits MINOR expression. Furthermore, Applicants acknowledge that the effects of DC-based vaccines are limited and the longevity of DCs needs to be extended before they can be successfully used as a vaccination in a subject.

The art teaches a population of dendritic cells for use in vaccination of a subject, wherein the dendritic cells comprise a siRNA agent which inhibits MINOR expression. See Wang et al. It is also noted that Wang et al. teach that mice vaccinated with DCs expressing MINOR siRNA ultimately died, and there was no significant difference in long-term survival, however inhibition of MINOR expression in the DC vaccines lead to

a significant delay in tumor progression (see Figure 4).

It is maintained that the art would not enable the disclosure of one dendrite cell-based vaccine to support claims directed to dendritic cells expressing *any* siRNA having substantial sequence homology to MINOR. Accordingly, one skilled in the art, being unable to use the art for such guidance, must necessarily find such guidance from the specification. However, one of skill would not find the guidance provided in the specification enough to overcome the unpredictability and challenges of using dendrite-based vaccines, as exemplified in the references above.

In order to practice the invention using the specification and the state of the art as outlined above, the quantity of experimentation required to practice the invention as claimed would require the *de novo* determination of those population of dendrites expressing MINOR siRNA that are successfully used as dendrite-based vaccinations against cancer, viral disease, bacterial disease, or immune disorders. Since the specification fails to provide any real guidance for a dendritic cell vaccine expressing a siRNA having substantial sequence homology to MINOR, other than SEQ ID NO:2 and SEQ ID NO:3, and since resolution of the various complications in regards to using dendritic-based vaccines is unpredictable, one of skill in the art would have been unable to practice the invention, commensurate in scope with the claims, without engaging in undue trial and error experimentation.

In view of the lack of guidance and working examples provided in the specification as filed, the level of unpredictability in the art in regards to using dendrite cell-based vaccines, and the breadth of the given claims, it is concluded that undue

experimentation would be required to practice the invention throughout the full scope of the claims, and therefore the invention is not fully enabled.

Conclusion

Claims 32 and 33 are allowable. Claims 32 and 33 are allowed because the prior art does not teach or fairly suggest a siRNA comprising SEQ ID NO:2 and SEQ ID NO:3 or a dendritic cell expressing SEQ ID NO:2 and SEQ ID NO:3.

Claim 36 is considered to be free of the prior art since the prior art does not teach or fairly suggest a population of dendritic cells for use in vaccination of a subject produced by the process of (a) obtaining dendritic cells from the subject; (b) causing the dendritic cells to express an antigen by either (i) exposing the dendritic cells to an antigen in culture under conditions promoting uptake and processing of the antigen, or (ii) transfecting the dendritic cells with a gene encoding an antigen; (c) activating the antigen-expressing dendritic cells; (d) treating the dendritic cells of (c) with an agent that inhibits mitogen induced nuclear orphan receptor (MINOR) expression, wherein the agent is a siRNA comprising SEQ ID NO:2 and SEQ ID NO:3.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached from 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fereydoun, Sajjadi can be reached on 571-272-3311. The fax phone number

for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.
For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

June 29, 2010
/Terra Cotta Gibbs/